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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	SEP 09	CA/CAplus records now contain indexing from 1907 to the present
NEWS 4	Jul 15	Data from 1960-1976 added to RDISCLOSURE
NEWS 5	Jul 21	Identification of STN records implemented
NEWS 6	Jul 21	Polymer class term count added to REGISTRY
NEWS 7	Jul 22	INPADOC: Basic index (/BI) enhanced; Simultaneous Left and Right Truncation available
NEWS 8	AUG 05	New pricing for EUROPATFULL and PCTFULL effective August 1, 2003
NEWS 9	AUG 13	Field Availability (/FA) field enhanced in BEILSTEIN
NEWS 10	AUG 15	PATDPAFULL: one FREE connect hour, per account, in September 2003
NEWS 11	AUG 15	PCTGEN: one FREE connect hour, per account, in September 2003
NEWS 12	AUG 15	RDISCLOSURE: one FREE connect hour, per account, in September 2003
NEWS 13	AUG 15	TEMA: one FREE connect hour, per account, in September 2003
NEWS 14	AUG 18	Data available for download as a PDF in RDISCLOSURE
NEWS 15	AUG 18	Simultaneous left and right truncation added to PASCAL
NEWS 16	AUG 18	FROSTI and KOSMET enhanced with Simultaneous Left and Righ Truncation
NEWS 17	AUG 18	Simultaneous left and right truncation added to ANABSTR
NEWS 18	SEP 22	DIPPR file reloaded
NEWS 19	SEP 25	INPADOC: Legal Status data to be reloaded
NEWS 20	SEP 29	DISSABS now available on STN

NEWS EXPRESS	OCTOBER 01 CURRENT WINDOWS VERSION IS V6.01a, CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP), AND CURRENT DISCOVER FILE IS DATED 23 SEPTEMBER 2003
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NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

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FILE 'HOME' ENTERED AT 14:03:18 ON 06 OCT 2003

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 14:03:28 ON 06 OCT 2003
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 3 OCT 2003 HIGHEST RN 598296-84-5
DICTIONARY FILE UPDATES: 3 OCT 2003 HIGHEST RN 598296-84-5

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2003

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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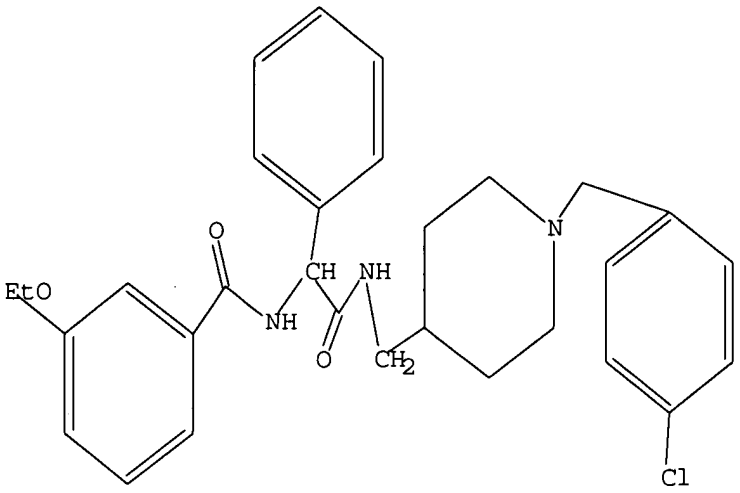

Structure attributes must be viewed using STN Express query preparation.

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FULL SCREEN SEARCH COMPLETED -    365 TO ITERATE

100.0% PROCESSED     365 ITERATIONS                          1 ANSWERS
SEARCH TIME: 00.00.01

L2            1 SEA SSS FUL L1

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FILE 'CAPLUS' ENTERED AT 14:04:05 ON 06 OCT 2003
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FILE COVERS 1907 - 6 Oct 2003  VOL 139 ISS 15
FILE LAST UPDATED: 5 Oct 2003  (20031005/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.
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L3            3 L2

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L3   ANSWER 1 OF 3  CAPLUS  COPYRIGHT 2003 ACS on STN
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DN   136:263090
TI   Preparation of cyclic amine derivatives for inhibition of the action of
     chemokines such as MIP-1.alpha. and/or MCP-1 on target cells
IN   Shiota, Tatsuki; Kataoka, Ken-Ichiro; Imai, Minoru; Tsutsumi, Takaharu;
     Sudoh, Masaki; Sogawa, Ryo; Morita, Takuya; Hada, Takahiko; Muroga,
     Yumiko; Takenouchi, Osami; Furuya, Minoru; Endo, Noriaki; Tarby, Christine
     M.; Moree, Wilna; Teig, Steven
PA   Teijin Limited, Japan; Dupont Pharmaceuticals Research Laboratories
SO   U.S., 364 pp., Cont. of U.S. Ser. No. 554,562.
     CODEN: USXXAM
DT   Patent
LA   English
FAN.CNT 2
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				WO 1998-US23254W 19981117

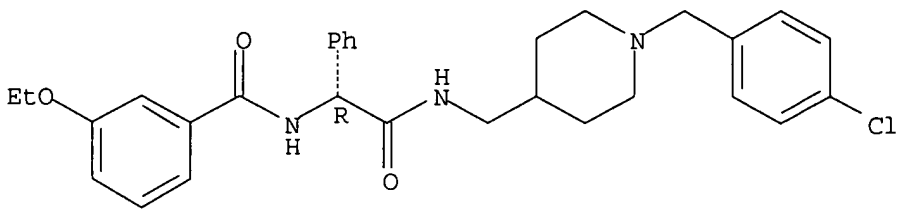
OS MARPAT 136:263090

IT **226248-06-2P**, Benzeneacetamide, N-[[1-[(4-chlorophenyl)methyl]-4-piperidinyl]methyl]-.alpha.-[(3-ethoxybenzoyl)amino]-, (.alpha.R)-
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of cyclic amine derivs. for inhibition of action of chemokines such as MIP-1.alpha. and/or MCP-1 on target cells)

RN 226248-06-2 CAPLUS

CN Benzeneacetamide, N-[[1-[(4-chlorophenyl)methyl]-4-piperidinyl]methyl]-.alpha.-[(3-ethoxybenzoyl)amino]-, (.alpha.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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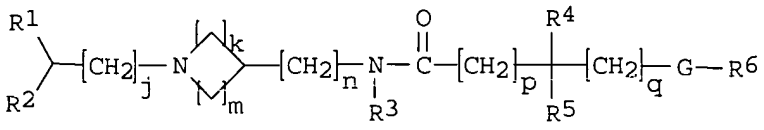

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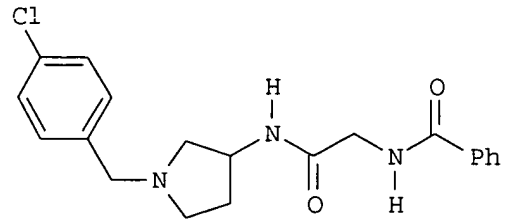

II

AB The title compds. [I; R1 = (un)substituted Ph, cycloalkyl, heteroaryl, etc.; R2 = H, alkyl, alkoxycarbonyl, etc.; j = 0-2; k = 0-2; m = 3-4 and k+m = 5 or 6; n = 0-1; R3 = H, alkyl; R4, R5 = H, OH, Ph, etc.; p, q = 0-1; G = CO, SO, CO2, etc.; R6 = Ph, cycloalkyl, cycloalkenyl, etc.] and their pharmaceutically acceptable acid addn. salts which inhibit the action of chemokines such as MIP-1.alpha. and/or MCP-1 on target cells and may be useful as a therapeutic drug and/or preventative drug in diseases, such as atherosclerosis, rheumatoid arthritis, and the like where blood monocytes and lymphocytes infiltrate into tissues, were prepd. Thus, reaction of N-benzoylglycine with 3-amino-1-(4-chlorobenzyl)pyrrolidine.2HCl in the presence of 3-ethyl-1-[3-(dimethylaminopropyl)]carbodiimide.HCl, 1-hydroxybenzotriazole and Et3N in CHCl3 afforded 95% II which showed 50-80% inhibition of MIP-1.alpha. binding to THP-1 cells at 10 .mu.M.

RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:824101 CAPLUS
DN 134:5154
TI Preparation of cyclic amine derivatives as remedies or preventives for diseases in association with chemokines or chemokine receptors
IN Shiota, Tatsuki; Miyagi, Fuminori; Kamimura, Takashi; Ohta, Tomohiro; Takano, Yasuhiro; Horiuchi, Hideki

PA Teijin Limited, Japan
SO PCT Int. Appl., 405 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000069432	A1	20001123	WO 2000-JP3203	20000518
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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				JP 1999-175856 A	19990518
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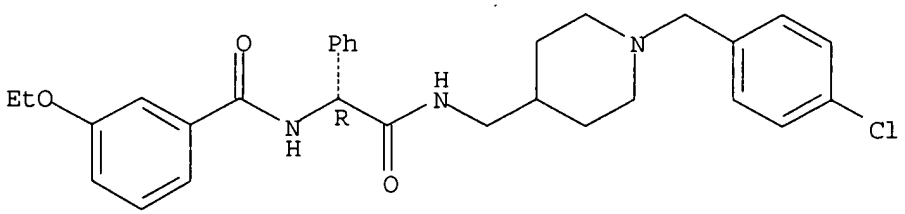
				WO 2000-JP3203 W	20000518

OS MARPAT 134:5154
IT **226248-06-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of cyclic amine derivs. as remedies or preventives for diseases in assocn. with chemokines or chemokine receptors)
RN 226248-06-2 CAPLUS
CN Benzeneacetamide, N-[[1-[(4-chlorophenyl)methyl]-4-piperidinyl]methyl]-.alpha.-[(3-ethoxybenzoyl)amino]-, (.alpha.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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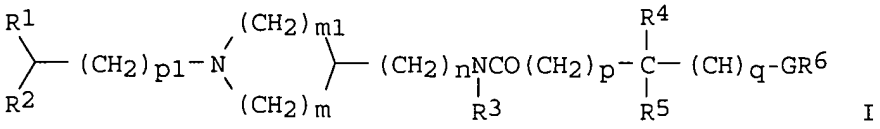

I

AB Remedies or preventives for diseases in assocn. with chemokines such as MIP-1.alpha. and/or MCP-1 or chemokine receptors such as CCR1 or CCR2 contain as the active ingredient N-acyl-amino acid N-cyclic amino or N-cyclic aminoalkyl-amide derivs. represented by general formula [I; (un)substituted Ph, C3-8 cycloalkyl, arom. heterocyclyl contg. 1-3 heteroatoms selected from O, S, and/or N; R2 = H, (un)substituted C1-6 alkyl, C2-7 alkoxycarbonyl, HO, (un)substituted Ph; p1, m1 = 0-2; m = 2-4; n = 0,1; R3 = H, (un)substituted C1-6 alkyl; R4, R5 = H, OH, (un)substituted Ph or C1-6 alkyl; or R4 and R5 are combined together to form a 3- to 5-membered hydrocarbyl; p, q = 0,1; G = CO, SO2, CO2, NR7CO, CONR7, NR7SO2, or SO2NR7, NHCONH, NHCSNH, NH CO2, O2CNH; R7 = H, C1-6 alkyl; or R7 and R5 are combined together to form C2-5 alkylene; R6 = (un)substituted Ph, C3-8 cycloalkyl, C3-6 cycloalkenyl, CH2Ph, or arom. heterocyclyl contg. 1-3 heteroatoms selected from O, S, and/or N, wherein Ph, CH2Ph, or arom. heterocyclyl group is optionally fused with (un)substituted benzene or arom. heterocyclyl contg. 1-3 heteroatoms selected from O, S, and/or N], pharmaceutically acceptable acid-adducts thereof, or pharmaceutically acceptable C1-6 alkyl-adducts thereof. The above diseases include destruction of bone or cartilage (e.g. arthritis, rheumatoid arthritis, osteoarthritis, osteoporosis, injury, and tumor), nephritis, kidney diseases, glomerulus or interstitial nephritis, nephrotic syndrome, demyelinating disease, or multiple sclerosis. Thus, N-3-ethoxybenzyl-D-methionine-N-[1-(4-chlorobenzyl)-4-piperazinylmethyl]amide in vitro inhibited the binding of human MIP-1.alpha. to THP-1 cells by >80% at 2 .mu.M.

RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:350650 CAPLUS
DN 131:18925
TI Preparation of cyclic amine derivatives for inhibition of the action of chemokines such as MIP-1.alpha. and/or MCP-1 on target cells
IN Shiota, Tatsuki; Kataoka, Kenichiro; Imai, Minoru; Tsutsumi, Takaharu; Sudoh, Masaki; Sogawa, Ryo; Morita, Takuya; Hada, Takahiko; Muroga, Yumiko; Takenouchi, Osami; Furuya, Monoru; Endo, Noriaki; Tarby, Christine M.; Moree, Wil A.; Teig, Steven L.
PA Teijin Ltd., Japan; Combichem, Inc.
SO PCT Int. Appl., 374 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9925686	A1	19990527	WO 1998-US23254	19981117

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PATENT FAMILY INFORMATION:

FAN 2002:237356

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OS MARPAT 131:18925

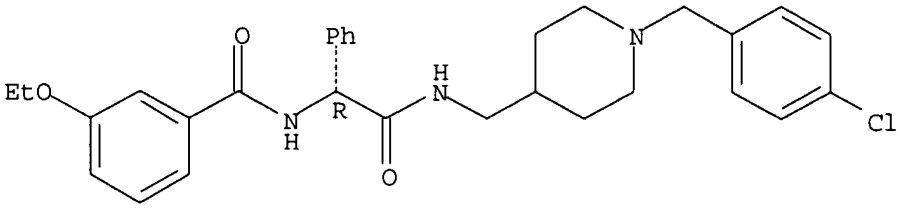
IT **226248-06-2P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of cyclic amine derivs. for inhibition of the action of chemokines such as MIP-1.alpha. and/or MCP-1 on target cells)

RN 226248-06-2 CAPLUS

CN Benzeneacetamide, N-[[1-[(4-chlorophenyl)methyl]-4-piperidinyl]methyl]-.alpha.-[(3-ethoxybenzoyl)amino]-, (.alpha.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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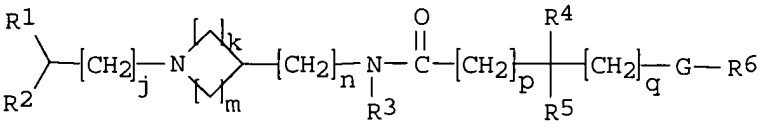

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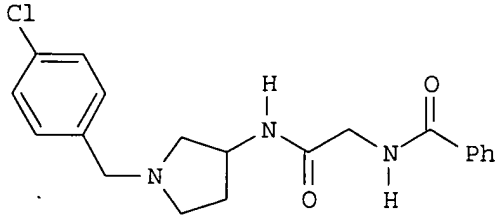

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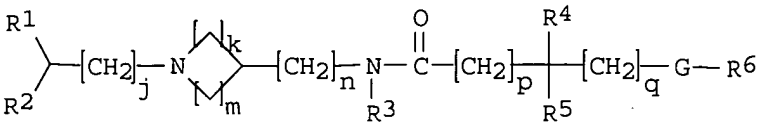

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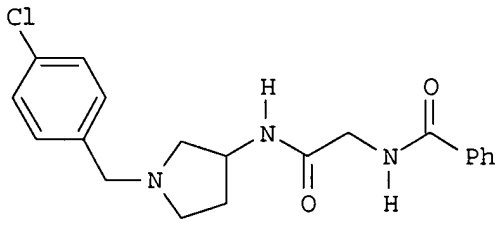

II

AB The title compds. [I; R1 = (un)substituted Ph, cycloalkyl, heteroaryl, etc.; R2 = H, alkyl, alkoxycarbonyl, etc.; j = 0-2; k = 0-2; m = 2-4; n = 0-1; R3 = H, alkyl; R4, R5 = H, OH< Ph, etc.; p = 0-1; q = 0-1; G = CO, SO, CO2, etc.; R6 = Ph, cycloalkyl, cycloalkenyl, etc.] and their pharmaceutically acceptable acid addn. salts which inhibit the action of chemokines such as MIP-1.alpha. and/or MCP-1 on target cells and may be useful as a therapeutic drug and/or preventative drug in diseases, such as atherosclerosis, rheumatoid arthritis, and the like where blood monocytes and lymphocytes infiltrate into tissues, were prepd. Thus, reaction of N-benzoylglycine with 3-amino-1-(4-chlorobenzyl)pyrrolidine.2HCl in the presence of 3-ethyl-1-[3-(dimethylaminopropyl)]carbodiimide.HCl, 1-hydroxybenzotriazole and Et3N in CHCl3 afforded 95% II which showed 50-80% inhibition of MIP-1.alpha. binding to THP-1 cells at 10 .mu.M.

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> s l3 and serine protease
L4            0 L3 AND SERINE PROTEASE

=> s serine protease and receptors
L5          750 SERINE PROTEASE AND RECEPTORS

=> s l5 and phenyl glycine
L6            0 L5 AND PHENYL GLYCINE

=> s l5 and piperidine
L7            0 L5 AND PIPERIDINE

=> s l5 and indole
L8            1 L5 AND INDOLE

=> d l8 fbib hitstr abs total

L8   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2003 ACS on STN
AN   1999:375527  CAPLUS
DN   131:31874
TI   Preparation of amidinophenylpropionylindoles and related compounds as
     thrombin inhibitors.
```

IN Heckel, Armin; Walter, Rainer; Soyka, Rainer; Stassen, Jean-Marie; Wienen, Wolfgang; Binder, Klaus
PA Boehringer Ingelheim Pharma KG, Germany
SO PCT Int. Appl., 173 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9928297	A1	19990610	WO 1998-EP7661	19981127
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RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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DE 19753522	A1	19990610	DE 1997-19753522	19971203
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OS MARPAT 131:31874
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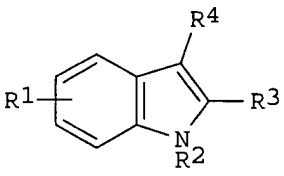

I

AB Title compds. [I; R1 = F, Cl, Br, CO2H, aminocarbonyl, aminosulfonyl, amino, group convertible to CO2H in vivo; 1 of R2, R4 = (CO2H- or group convertible to CO2H in vivo-substituted) alkyl, the other = R5A; A = (CO2H- or group convertible to CO2H in vivo-substituted) alkylene, etc.; R5 = R6NHC(:NH)-substituted Ph; R4 = H, alkyl; R6 = H, in vivo-cleavable group], were prepd. as antithrombotics with inhibitory activity against **serine proteases** XII and fibrinogen **receptors**. Thus, 3-[3-(4-amidinophenyl)propionyl]-1-methylindole-5-carboxylic acid N-(2-carboxyethyl)-N-phenylamide hydrochloride (prepn. given) showed a thrombin time ED200 = 0.80 .mu.M.
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s l5 indole and piperidine
MISSING OPERATOR L5 INDOLE
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s l5 and indole and piperidine
L9 0 L5 AND INDOLE AND PIPERIDINE

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=> log y
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                              50.38     198.74

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)    SINCE FILE      TOTAL
                                                 ENTRY    SESSION
CA SUBSCRIBER PRICE                              -2.60      -2.60

STN INTERNATIONAL LOGOFF AT 14:09:10 ON 06 OCT 2003
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Welcome to STN International! Enter x:x

LOGINID:ssspta1611sxp

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	SEP 09	CA/CAplus records now contain indexing from 1907 to the present
NEWS 4	Jul 15	Data from 1960-1976 added to RDISCLOSURE
NEWS 5	Jul 21	Identification of STN records implemented
NEWS 6	Jul 21	Polymer class term count added to REGISTRY
NEWS 7	Jul 22	INPADOC: Basic index (/BI) enhanced; Simultaneous Left and Right Truncation available
NEWS 8	AUG 05	New pricing for EUROPATFULL and PCTFULL effective August 1, 2003
NEWS 9	AUG 13	Field Availability (/FA) field enhanced in BEILSTEIN
NEWS 10	AUG 15	PATDPAFULL: one FREE connect hour, per account, in September 2003
NEWS 11	AUG 15	PCTGEN: one FREE connect hour, per account, in September 2003
NEWS 12	AUG 15	RDISCLOSURE: one FREE connect hour, per account, in September 2003
NEWS 13	AUG 15	TEMA: one FREE connect hour, per account, in September 2003
NEWS 14	AUG 18	Data available for download as a PDF in RDISCLOSURE
NEWS 15	AUG 18	Simultaneous left and right truncation added to PASCAL
NEWS 16	AUG 18	FROSTI and KOSMET enhanced with Simultaneous Left and Righ Truncation
NEWS 17	AUG 18	Simultaneous left and right truncation added to ANABSTR
NEWS 18	SEP 22	DIPPR file reloaded
NEWS 19	SEP 25	INPADOC: Legal Status data to be reloaded
NEWS 20	SEP 29	DISSABS now available on STN

NEWS EXPRESS	OCTOBER 01 CURRENT WINDOWS VERSION IS V6.01a, CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP), AND CURRENT DISCOVER FILE IS DATED 23 SEPTEMBER 2003
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NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

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FILE 'HOME' ENTERED AT 14:13:27 ON 06 OCT 2003

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FILE 'REGISTRY' ENTERED AT 14:13:36 ON 06 OCT 2003
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 3 OCT 2003 HIGHEST RN 598296-84-5
DICTIONARY FILE UPDATES: 3 OCT 2003 HIGHEST RN 598296-84-5

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Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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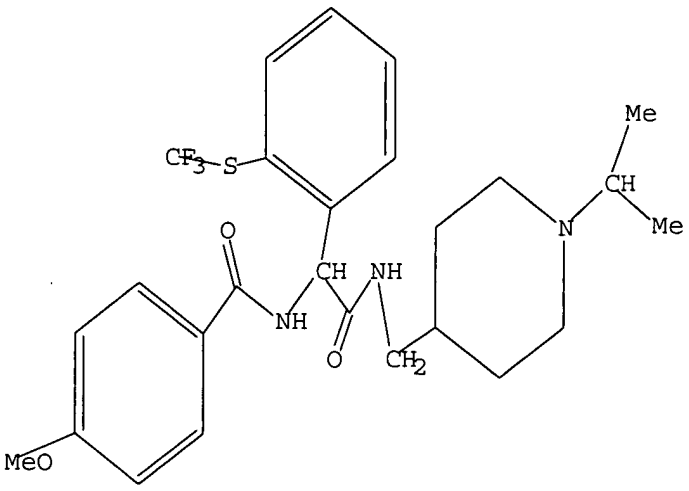

Structure attributes must be viewed using STN Express query preparation.

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FULL SCREEN SEARCH COMPLETED - 24 TO ITERATE

100.0% PROCESSED 24 ITERATIONS 1 ANSWERS
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L2 1 SEA SSS FUL L1

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
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USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 6 Oct 2003 VOL 139 ISS 15
FILE LAST UPDATED: 5 Oct 2003 (20031005/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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AN   2001:923765  CAPLUS
DN   136:37947
TI   Preparation of amino acid derivatives as serine protease inhibitors
IN   Liebeschuetz, John Walter; Murray, Christopher William; Young, Stephen
     Clinton; Camp, Nicholas Paul; Jones, Stuart Donald; Wylie, William
     Alexander; Masters, John Joseph; Wiley, Michael Robert; Sheehan, Scott
     Martin; Engel, David Birenbaum; Watson, Brian Morgan
PA   Eli Lilly and Company, USA
SO   PCT Int. Appl., 188 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 13
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     US 2003109706       A1    20030612      US 2002-30188    20020204
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GB 2000-30305 A 20001213
WO 2001-GB2551 W 20010612

PATENT FAMILY INFORMATION:

FAN 1999:184268

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				GB 1998-3173	A 19980213
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				GB 1998-3173	A 19980213
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FAN 1999:184269

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FAN 2000:900613

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FAN 2000:900614

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GB 1999-13823 A 19990614
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EP 1192132 A2 20020403 EP 2000-938916 20000613
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WO 2000-GB2302 W 20000613
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NO 2002005665 A 20021125 NO 2002-5665 20021125
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FAN 2000:900663

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PI	WO 2000077027	A2	20001221	WO 2000-GB2291	20000613
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FAN 2001:453049

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				WO 2000-GB2291	W 20000613
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FAN 2001:923758

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2000076971 A2 20001221 WO 2000-GB2302 20000613
WO 2000076971 A3 20010802
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				WO 2000-GB2302 W	20000613
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				WO 2001-GB2541 W	20010612

FAN 2001:923766

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PI	WO 2001096304	A1	20011220	WO 2001-GB2572	20010612

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				WO 2000-GB2302 W	20000613
				GB 2000-30306 A	20001213
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				GB 2000-30306 A	20001213
				WO 2001-GB2572 W	20010612

FAN 2001:923784

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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				WO 2000-GB2302 W 20000613
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				GB 1999-29553 A 19991214
	EP 1289972	A1	20030312	EP 2001-936686 20010612
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
				WO 2000-GB2302 A 20000613
				GB 2000-30304 A 20001213
				WO 2001-GB2553 W 20010612
	BR 2001011451	A	20030624	BR 2001-11451 20010612
				WO 2000-GB2302 A 20000613
				GB 2000-30304 A 20001213
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	US 2003055246	A1	20030320	US 2002-30187 20020204
				GB 2000-30304 A 20001213
				WO 2001-GB2553 W 20010612
	WO 2002100847	A2	20021219	WO 2002-US16569 20020606
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				WO 2001-GB2553 W 20010612
				US 2001-339295PP 20011212
	NO 2002005665	A	20021125	NO 2002-5665 20021125
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				WO 2001-GB2553 W 20010612

FAN 2002:354079

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002055522	A1	20020509	US 2001-988082	20011119
				GB 1997-18392 A	19970829
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				WO 1998-GB2605 W	19980828
				GB 1999-13823 A	19990614
				US 1999-142064PP	19990702
				US 2000-485678 A2	20000225

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WO 2000077027 A2 20001221 WO 2000-GB2291 20000613

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

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FAN 2002:465859

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI WO 2002047762 A1 20020620 WO 2001-GB5526 20011212

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

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WO 2000-GB4764 W 20001213

GB 2001-14185 A 20010612

WO 2001044226 A1 20010621 WO 2000-GB4764 20001213

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

GB 1999-29552 A 19991214

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AU 2002022207 A5 20020624 AU 2002-22207 20011212

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EP 1343561 A1 20030917 EP 2001-270360 20011212
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
WO 2000-GB4764 A 20001213
GB 2001-14185 A 20010612
WO 2001-GB5526 W 20011212

FAN 2002:964343

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002100847	A2	20021219	WO 2002-US16569	20020606
WO 2002100847	A3	20030821		

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
WO 2001-GB2553 W 20010612
US 2001-339295PP 20011212

WO 2001096323 A1 20011220 WO 2001-GB2553 20010612
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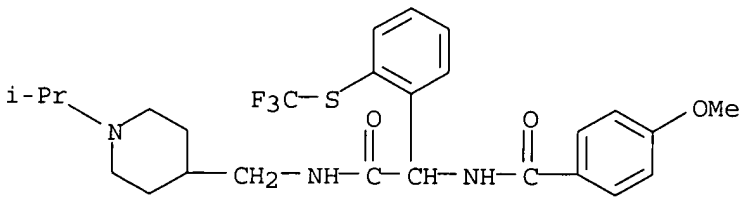
WO 2000-GB2302 W 20000613
GB 2000-30304 A 20001213

OS MARPAT 136:37947

IT **380900-59-4P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of amino acid derivs. as serine protease inhibitors)

RN 380900-59-4 CAPLUS

CN Benzeneacetamide, .alpha.-[(4-methoxybenzoyl)amino]-N-[[1-(1-methylethyl)-4-piperidinyl]methyl]-2-[(trifluoromethyl)thio]- (9CI) (CA INDEX NAME)



AB Compds. R2-X-X-Y(Cy)-L-Lp(D)n [R2 is a 5- or 6-membered arom. carbon ring

optionally interrupted by a N, O or S ring atom, optionally substituted at the 3 and/or 4 position or forms a fused ring system at these positions, which is an optionally substituted 5- or 6-membered carbocyclic or heterocyclic ring, or substituted at the position alpha to X-X; X is a C, N, O or S atom or a CO, CR1a, C(R1a)2 or NR1a group, where R1a represents H, OH, alkoxy, alkyl, aminoalkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, alkylaminocarbonyl, alkoxycarbonylamino, acyloxymethoxycarbonyl or alkylamino optionally substituted by OH, alkylamino, alkoxy, oxo, aryl or cycloalkyl; Y is a N atom or a CR1b group (R1b defined as for R1a); Cy is an (un)substituted, (un)satd., mono- or polycyclic, homo- or heterocyclic group; L is an org. linker group contg. 1 to 5 backbone atoms selected from C, N, O and S, or a branched alkyl or cyclic group; -Lp(D)n is 1-[R10-(Lb)u-(G)t-(La)s]-3-pyrrolidinyl or -4-piperidinyl, where s, t and u = 0 or 1; La and Lb is a single bond, CO, O, NH or alkylimino; G = alkanediyl; R10 = alkyl, cycloalkyl, indanyl, pyridyl, tetrahydropyranyl, (un)substituted Ph, etc.] or their physiol.-tolerable salts were prepd. for use as serine protease and factor Xa inhibitors in the treatment of cardiovascular disorders. Compds. of the invention were found to significantly elongate the partial thromboplastin time (prothrombin time). Thus, 4-[(4-methoxybenzoyl-D-phenylglycinyl)aminomethyl]-1-isopropylpiperidine was prepd. in the first of 106 examples.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s serine protease and Thrombolic disorders
L4 0 SERINE PROTEASE AND THROMBOLIC DISORDERS

=> s serine protease and factor xa
L5 527 SERINE PROTEASE AND FACTOR XA

=> s l5 and Thrombotic disorders
L6 7 L5 AND THROMBOTIC DISORDERS

=> d l6 fbib hitstr abs total

L6 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:634690 CAPLUS
TI SAR investigation on the in-vitro metabolism of 1,2-aminoethanol-derived non-covalent **factor Xa** inhibitors
AU Sheehan, Scott M.; Watson, Brian M.; Wiley, Michael R.; Liebeschuetz, J. W.; Sall, Daniel J.; Franciskovich, Jeffry B.; Marimuthu, Jothirajah; Smallwood, Jeffrey K.; Patel, Nita J.; Woodland, Joseph; Barbuch, Robert; Craft, Trelia J.; Gifford-Moore, Donetta; Farmen, Mark W.; Towner, Richard D.; Smith, Gerald F.
CS Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN, 46285, USA
SO Abstracts of Papers, 226th ACS National Meeting, New York, NY, United States, September 7-11, 2003 (2003), MEDI-082 Publisher: American Chemical Society, Washington, D. C.
CODEN: 69EKY9
DT Conference; Meeting Abstract
LA English
AB The trypsin-like **serine protease factor Xa** (fXa) plays a key role in the coagulation cascade and is responsible for the conversion of prothrombin to thrombin. As a result, inhibition of fXa has emerged as a promising approach for the treatment of

thrombotic disorders. We have recently discovered a series of novel 1,2-aminoethanol-derived **factor Xa** inhibitors and we investigated the surrogate metabolic profile of these derivs. Metabolite identification studies have revealed sites of potential oxidative metab. In this presentation, the synthesis of these 1,2-aminoethanol-derived fXa inhibitors and their corresponding enzyme inhibitory activity will be disclosed. Discussion will focus on the impact of inhibitor structural modification on obsd. surrogate metab. in human, rat, dog, and monkey microsomes.

L6 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:709216 CAPLUS
DN 134:231346
TI An update on heparins at the beginning of the new millennium
AU Fareed, Jawed; Hoppensteadt, Debra A.; Bick, Rodger L.
CS Hemostasis & Thrombosis Research Laboratories, Department of Pathology and Pharmacology, Loyola University Medical Center, Maywood, IL, 60153, USA
SO Seminars in Thrombosis and Hemostasis (2000), 26(Suppl. 1), 5-21
CODEN: STHMBV; ISSN: 0094-6176
PB Thieme Medical Publishers, Inc.
DT Journal; General Review
LA English
AB A review with 35 refs. Unfractionated heparin has enjoyed the sole anticoagulant status for almost half a century. Besides an effective anticoagulant, this drug has been used in several addnl. indications. Despite the development of newer anticoagulant drugs, unfractionated heparin has remained the drug of choice for surgical anticoagulation and interventional cardiol. In the area of hematol. and transfusion medicine, unfractionated heparin has continued to play a major role as an anticoagulant drug. The development of low-mol.-wt. heparins (LMWHs) represents a refinement for the use of heparin. These drugs represent a class of depolymd. heparin derivs. with a distinct pharmacol. profile that is largely detd. by their compn. These drugs produce their major effects by combining with antithrombin and exerting antithrombin and anti-Xa inhibition. In addn., the LMWHs also increase non-antithrombin-dependent effects such as TFPI release, modulation of adhesion mols., and release of pro-fibrinolytic and antithrombotic mediators from the blood vessels. The cumulative effects of each of the different LMWHs differ and each product exhibits a distinct profile. Initially these agents were developed for the prophylaxis of postsurgical deep-vein thrombosis. However, at this time these drugs are used not only for prophylaxis, but also for the treatment of **thrombotic disorders** of both the venous and arterial type. To a large extent, the LMWHs have replaced unfractionated heparin in most s.c. indications. With the use of these refined heparins, outpatient anticoagulant management has gone through a dramatic evolution. For the first time, patients with **thrombotic disorders** can be treated in an outpatient setting. Thus, the introduction of LMWHs represents a major advance in improving the use of heparin. The development of the oral formulation of heparin and LMWHs also provides an important area that may impact on the use of heparin and LMWHs. The increased awareness of heparin-induced thrombocytopenia has necessitated the development of newer methods to identify patients at risk of developing this catastrophic syndrome. Furthermore, a strong interest has developed in alternate drugs or the management of patients with this syndrome. Despite the development of alternate anticoagulants that are mostly antithrombin derived (hirudins, hirulog), these agents have failed to provide similar clin. outcome as heparin in many indications. However, antithrombin drugs are useful in the anticoagulant management of

heparin-compromised patients. The FDA has approved a recombinant hirudin (Refludan) and a synthetic antithrombin agent, argatroban (Novastan), for this indication. The development of synthetic heparin pentasaccharide and anti-Xa agents may have an impact on the prophylaxis of **thrombotic disorders**. However, these monotherapeutic agents do not mimic the polytherapeutic actions of heparin. Furthermore, these agents do not inhibit thrombin. Heparin and LMWHs are capable of inhibiting not only **factor Xa** and thrombin, but other **serine proteases** in the coagulation network. The only way the newer drugs can mimic the actions of heparin is in combination modalities (polytherapeutic approaches). It has been suggested that newer antiplatelet drugs also exhibit anticoagulant actions. While these drugs may exhibit weak effects on thrombin generation, none of the currently available antiplatelet drugs exhibit any degree of antithrombin actions. It is likely that heparins synergize or augment the effects of the new antiplatelet drugs. Currently, combination approaches are used to anticoagulate patients in these studies. The dosage of heparins has been arbitrarily reduced. This may not be an optimal procedure. Addnl. clin. studies are needed to study these. Combinations where the alterations of these drugs are compared. Such combinations will require newer monitoring approaches. The development of oral thrombin agents, GP IIb/IIIa inhibitors, has met with some significant obstacles. Thus, it is unlikely that this approach will be very feasible in the indications where heparins are used. It is fair to state that heparins will continue to play a major role in the overall management of **thrombotic disorders** in monotherapeutic and polytherapeutic modalities.

RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:640853 CAPLUS
DN 131:271815
TI Preparation of 2(1H)-quinolinones as **serine protease** inhibitors for treatment of **thrombotic disorders**
IN Dudley, Danette Andrea; Edmunds, Jeremy John
PA Warner-Lambert Co., USA
SO PCT Int. Appl., 136 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9950263	A1	19991007	WO 1998-US26709	19981215
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	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
				US 1998-80090P P	19980331
	CA 2312953	AA	19991007	CA 1998-2312953	19981215
				US 1998-80090P P	19980331
				WO 1998-US26709W	19981215
	AU 9919184	A1	19991018	AU 1999-19184	19981215
	AU 763110	B2	20030710		
				US 1998-80090P P	19980331

				WO 1998-US26709W 19981215
BR 9815786	A	20001121	BR 1998-15786	19981215
			US 1998-80090P P	19980331
			WO 1998-US26709W	19981215
EP 1091955	A1	20010418	EP 1998-963966	19981215
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			US 1998-80090P P	19980331
			WO 1998-US26709W	19981215
JP 2002509928	T2	20020402	JP 2000-541167	19981215
			US 1998-80090P P	19980331
			WO 1998-US26709W	19981215
NZ 505921	A	20030829	NZ 1998-505921	19981215
			US 1998-80090P P	19980331
			WO 1998-US26709W	19981215
ZA 9902448	A	20001011	ZA 1999-2448	19990330
			US 1998-80090P P	19980331
NO 2000004696	A	20000920	NO 2000-4696	20000920
			US 1998-80090P P	19980331
			WO 1998-US26709W	19981215

OS MARPAT 131:271815

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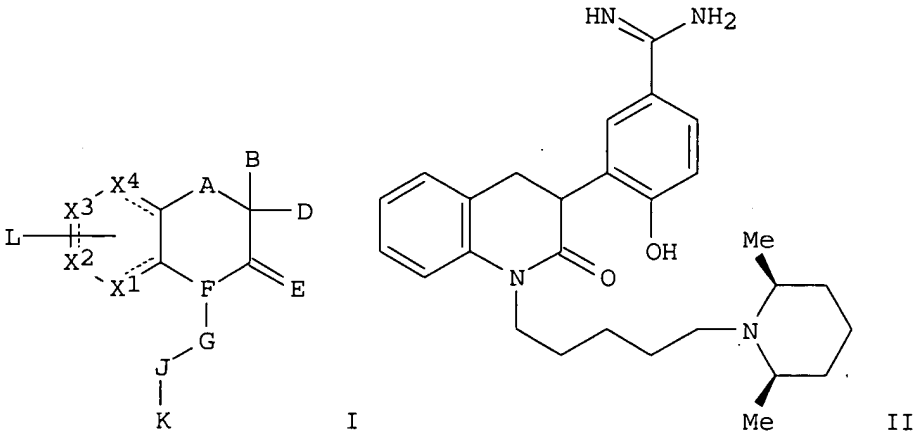

I II

AB 2(1H)-Quinolinones (I) [where A = CH2, CH, or C(alkyl); B and D = independently H, (un)substituted (cyclo)alkyl, hetero(cyclo)alkyl, aryl(alkyl), or heterocycle; E = absent or O, S, or NH; F = N, NCH2, or CH2N; G and (un)substituted K = independently absent or (cyclo)alkyl interrupted by 1 or more heteroatoms; J = absent or (un)substituted aryl or heterocycle; L = H, halogen, OH, (un)substituted alkoxy, alkyl, amino, etc.; X1-X4 = independently C or N], which display inhibitory effects on **serine proteases** such as **factor Xa**, thrombin and/or factor VIIa, were prepd. For example, 1,5-dibromopentane was added to 4-(benzyloxy)-3-(2-oxo-1,2,3,4-tetrahydro-3-quinolinyl)benzenecarbonitrile (5-step prepn. given) to yield the N-substituted tetrahydroquinolinone. Cis-2,6-dimethylpiperidine was added to the 5-bromopentylquinolinone to form the piperidinylpentyl deriv. This intermediate was converted to the title quinolinone II.2HCl by treatment

with NH2OH.HCl followed by addn. of CF3CO2H and redn. with Pd/C. Typically, the compds. of the invention showed 50% inhibition of **factor Xa** proteolytic activity on a synthetic substrate in concns. ranging from 50 .mu.M to 1 nM. II demonstrated inhibitory activity in std. assays of thrombin (IC50 = 1.14 .mu.M), trypsin (IC50 = 0.562 .mu.M), and **factor Xa** (IC50 = 0.02 .mu.M). Compds. of the invention are claimed to be useful in the treatment or prevention of venous and arterial thrombosis, pulmonary embolism, myocardial and cerebral infarction, restenosis, cancer, angina, diabetes, heart failure, and atrial fibrillation in mammals.

RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:640844 CAPLUS
DN 131:271886
TI Preparation of quinoxalinones as **serine protease** inhibitors for treatment of **thrombotic disorders**
IN Dudley, Danette Andrea; Edmunds, Jeremy John
PA Warner-Lambert Co., USA
SO PCT Int. Appl., 104 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9950254	A1	19991007	WO 1998-US26704	19981215
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HR, HU, ID, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
			US 1998-80042P P	19980331
CA 2319554	AA	19991007	CA 1998-2319554	19981215
			US 1998-80042P P	19980331
			WO 1998-US26704W	19981215
AU 9919179	A1	19991018	AU 1999-19179	19981215
			US 1998-80042P P	19980331
			WO 1998-US26704W	19981215
BR 9815785	A	20001205	BR 1998-15785	19981215
			US 1998-80042P P	19980331
			WO 1998-US26704W	19981215
EP 1068190	A1	20010117	EP 1998-963961	19981215
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			WO 1998-US26704W	19981215
ZA 9902447	A	20001010	ZA 1999-2447	19990330
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US 6410536	B1	20020625	US 2000-601606	20000803
			US 1998-80042P P	19980331
NO 2000004697	A	20000920	NO 2000-4697	20000920
			US 1998-80042P P	19980331
			WO 1998-US26704W	19981215
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US 2000-601606 A320000803

OS MARPAT 131:271886
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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB 2(1H)-Quinoxalinones (I) [where A = N, N(alkyl)CH2, CH2N(alkyl), NO; B and D = independently H, (un)substituted (cyclo)alkyl, hetero(cyclo)alkyl, aryl(alkyl), or heterocycle; E = absent or O, S, or NH; F = N, NCH2, or CH2N; G and (un)substituted K = independently absent or (cyclo)alkyl interrupted by 1 or more heteroatoms; J = absent or (un)substituted aryl or heterocycle; L = H, halogen, OH, (un)substituted alkoxy, alkyl, amino, etc.; X1-X4 = independently C or N], which display inhibitory effects on **serine proteases** such as **factor Xa**, thrombin, trypsin, and/or factor VIIa, were prepd. For example, 1,5-dibromopentane was added to 4-(benzyloxy)-3-(3-oxo-3,4-dihydro-2-quinoxalinyl)benzenecarbonitrile (6-step prepn. given) to yield the N-substituted dihydroquinoxaline. Cis-2,6-dimethylpiperidine was added to the 5-bromopentylquinoxalinone to form the piperidinylpentyl deriv. This intermediate was debenzylated and the nitrile converted to the carboximidamide to form the title quinoxalinone (II).2HCl. Typically, the compds. of the invention showed 50% inhibition of **factor Xa** proteolytic activity on a synthetic substrate in concns. ranging from 50 .mu.M to 1 nM. II demonstrated inhibitory activity in std. assays of thrombin (IC50 = 2.96 .mu.M), trypsin (IC50 = 2.03 .mu.M), and **factor Xa** (IC50 = 0.065 .mu.M). At a concn. of 100 .mu.M, II inhibited the catalytic activity of human tissue factor/factor VIIa complex by 16%. In an in vitro assay, II demonstrated human prothrombinase (PTase) complex inhibition with an IC50 of 0.0015 .mu.M. The effects of II on thrombosis and hemostasis was studied in a rabbit veno-venous shunt model and in a dog electrolytic injury model of thrombosis. At the highest dose, II prolonged a PTT and PT by a 5- and 3.9-fold, resp., for the veno-venous shunt model and by 1.4- and 1.75-fold, resp., for the electrolytic injury model. Compds. of the invention are claimed to be useful in the treatment or prevention of venous and arterial thrombosis, pulmonary embolism, myocardial and cerebral infarction, restenosis, cancer, angina, diabetes, heart failure, and atrial fibrillation in mammals.

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1998:141160 CAPLUS
TI Design, synthesis and biological activity of novel **factor Xa** inhibitors. 10. Optimization of dibenzyl cyclic urea analogs.
AU Chou, Y.-L.; Guilford, W. J.; Koovakkat, S.; Mohan, R.; Wu, S. C.; Liang, A.; Trinh, L.; Morrissey, M. M.
CS Berlex Biosciences, Richmond, CA, 94804, USA
SO Book of Abstracts, 215th ACS National Meeting, Dallas, March 29-April 2 (1998), MEDI-130 Publisher: American Chemical Society, Washington, D. C. CODEN: 65QTAA
DT Conference; Meeting Abstract
LA English

AB Inhibitors of **factor Xa**, a **serine protease** involved in the coagulation cascade, are being developed both for the treatment and prevention of **thrombotic disorders**. Compds. 1 and 2 are novel **factor Xa** inhibitors that display selectivity over other **serine proteases** in the coagulation cascade. The synthesis and SAR of these compds. will be described.

L6 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1998:31312 CAPLUS
DN 128:102394
TI Preparation of pyrrolo[1,2-a]pyrazine-1,4-dione **serine protease** inhibitors
IN Berryman, Kent Alan; Doherty, Annette Marian; Edmunds, Jeremy John; Siddiqui, M. Arshad
PA Warner-Lambert Co., USA; Berryman, Kent Alan; Doherty, Annette Marian; Edmunds, Jeremy John; Siddiqui, M. Arshad
SO PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9748706	A1	19971224	WO 1997-US9832	19970610
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RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
			US 1996-19989P P	19960618
AU 9732325	A1	19980107	AU 1997-32325	19970610
			US 1996-19989P P	19960618
			WO 1997-US9832 W	19970610
US 6124291	A	20000926	US 1998-171863	19981027
			US 1996-19989P P	19960618
			WO 1997-US9832 W	19970610

OS MARPAT 128:102394
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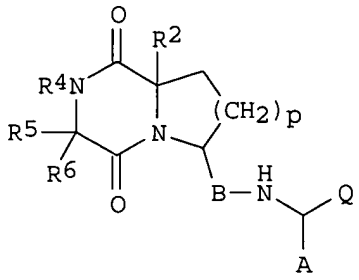

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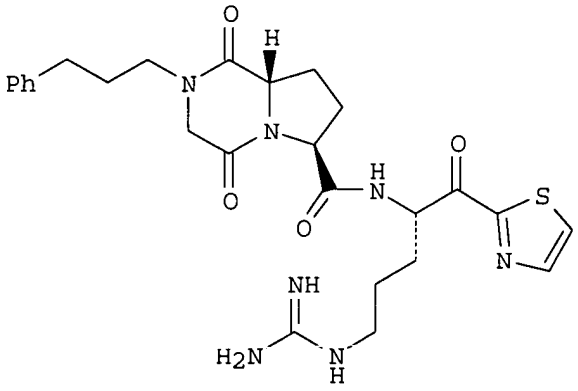

II

AB This invention relates to pyrrolo[1,2-a]pyrazine-1,4-diones I (B = CO, CH2; R2, R4, R5, R6 = independently H, alkyl, substituted alkyl; A = basic group; Q = H, keto heterocycle group; p = 0-2). The compds. are inhibitors of **serine proteases**, typically thrombin, **Factor Xa**, and Factor VIIa, and are useful for treating and preventing **thrombotic disorders**. Thus, title deriv. II was prepd. in 14 steps from Z-Asp-OCMe3 (Z = PhCH2O2C), Ph(CH2)3-Gly-OCH2Ph, Boc-Arg(Mtr)-OH (Boc = Me3CO2C; Mtr = 4-methoxy-2,3,6-trimethylphenylsulfonyl), and thiazole.II inhibited thrombin with Ki = 3 nM, **factor Xa** at 30 nM, and trypsin <1 nM.

L6 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1995:76729 CAPLUS
DN 122:229811
TI **Factor Xa** inhibitors
AU Mao, Shi-Shan
CS Merck Research Laboratories, Department Biological Chemistry, West Point, PA, 19486, USA
SO Perspectives in Drug Discovery and Design (1994), 1(3), 423-30
CODEN: PDDDEC; ISSN: 0928-2866
DT Journal; General Review
LA English
AB A review with 50 refs. **Factor Xa** is the **serine protease** that activates prothrombin to yield thrombin. Inhibitors of **factor Xa** play a crucial role in curtailing thrombin generation. Two key **factor Xa** inhibitors that are found in blood are antithrombin III and tissue factor pathway inhibitor. Inhibition of **factor Xa** is a mechanism that is also exploited by certain hematophagous animals to

facilitate feeding. Evaluation of tick anticoagulant peptide (TAP) and leech-derived antistasin (ATS) using animal models of **thrombotic disorders** has confirmed that specific blockade of **factor Xa** activity is an effective antithrombotic strategy. Several labs. are currently pursuing low-mol. wt. synthetic **factor Xa** inhibitors for use as anticoagulants in the treatment and/or prevention of thrombosis.

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L7            1 L5 AND L3

=> d his

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L2             1 S L1 SSS FULL

     FILE 'CAPLUS' ENTERED AT 14:14:09 ON 06 OCT 2003
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L4             0 S SERINE PROTEASE AND  THROMBOLIC DISORDERS
L5           527 S SERINE PROTEASE AND FACTOR XA
L6             7 S L5 AND THROMBOTIC DISORDERS
L7             1 S L5 AND L3

=> d l7 fbib hitstr abs total

L7   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2003 ACS on STN
AN   2001:923765  CAPLUS
DN   136:37947
TI   Preparation of amino acid derivatives as serine protease
     inhibitors
IN   Liebeschuetz, John Walter; Murray, Christopher William; Young, Stephen
     Clinton; Camp, Nicholas Paul; Jones, Stuart Donald; Wylie, William
     Alexander; Masters, John Joseph; Wiley, Michael Robert; Sheehan, Scott
     Martin; Engel, David Birenbaum; Watson, Brian Morgan
PA   Eli Lilly and Company, USA
SO   PCT Int. Appl., 188 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 13
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PI   WO 2001096303      A1    20011220      WO 2001-GB2551   20010612
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             BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                                         WO 2000-GB2302 W 20000613
                                         GB 2000-30305  A 20001213
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WO 2000076971	A2	20001221	WO 2000-GB2302	20000613
WO 2000076971	A3	20010802		

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		GB 1999-13823	A 19990614
		US 1999-142064P	P 19990702
		GB 1999-18741	A 19990809
		GB 1999-29553	A 19991214
EP 1289954	A1	20030312	EP 2001-940716 20010612

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		WO 2000-GB2302	A 20000613
		GB 2000-30305	A 20001213
		WO 2001-GB2551	W 20010612
US 2003109706	A1	20030612	US 2002-30188 20020204
		WO 2000-GB2302	A 20000613
		GB 2000-30305	A 20001213
		WO 2001-GB2551	W 20010612

PATENT FAMILY INFORMATION:

FAN 1999:184268

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9911657	A1	19990311	WO 1998-GB2600	19980828

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		GB 1997-18392	A 19970829
		GB 1998-3173	A 19980213
AU 9888753	A1	19990322	AU 1998-88753 19980828
		GB 1997-18392	A 19970829
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		WO 1998-GB2600	W 19980828
EP 1012166	A1	20000628	EP 1998-940425 19980828

R: CH, DE, ES, FR, GB, IT, LI, NL

		GB 1997-18392	A 19970829
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US 6262069	B1	20010717	US 2000-485677 20000225
		GB 1997-18392	A 19970829
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		WO 1998-GB2600	W 19980828
		US 2000-485677	A1 20000225

	US 6420438	B1	20020716	US 2000-865418	20010529
				WO 1998-GB2600 W	19980828
				US 2000-485677 A1	20000225

FAN 1999:184269

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PI	WO 9911658	A1	19990311	WO 1998-GB2605	19980828

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	AU 9888757	A1	19990322	AU 1998-88757	19980828
				GB 1997-18392 A	19970829
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R: DE, FR, GB, IT

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				GB 1997-18392 A	19970829
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				GB 1999-13823 A	19990614
				US 1999-142064PP	19990702
				US 2000-485678 A2	20000225
				WO 2000-GB2291 A2	20000613

FAN 2000:900613

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PI	WO 2000076970	A2	20001221	WO 2000-GB2296	20000613
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				GB 1999-29552 A	19991214
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FAN 2000:900614

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GB 1999-13823 A 19990614
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FAN 2000:900663

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				GB 1999-18741	A 19990809
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FAN 2001:453049

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WO 2000-GB4764 W 20001213

EP 1294691 A1 20030326 EP 2001-938399 20010612
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WO 2001-GB2566 W 20010612

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FAN 2001:923758

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WO 2000-GB2302 W 20000613
GB 2000-30303 A 20001213

WO 2000076971 A2 20001221 WO 2000-GB2302 20000613
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GB 1999-13823 A 19990614
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GB 1999-29553 A 19991214

EP 1289950 A1 20030312 EP 2001-938386 20010612
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GB 2000-30303 A 20001213
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US 2003078438 A1 20030424 US 2002-30189 20020204
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GB 2000-30303 A 20001213
WO 2001-GB2541 W 20010612

FAN 2001:923766

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PI WO 2001096304 A1 20011220 WO 2001-GB2572 20010612
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WO 2000076971 A2 20001221 WO 2000-GB2302 20000613
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FAN	2001:923784				
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WO 2000-GB2302 A 20000613
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FAN 2002:354079

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WO 2000077027 A2 20001221 WO 2000-GB2291 20000613
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CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
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FAN 2002:465859

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FAN 2002:964343

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002100847	A2	20021219	WO 2002-US16569	20020606
WO 2002100847	A3	20030821		

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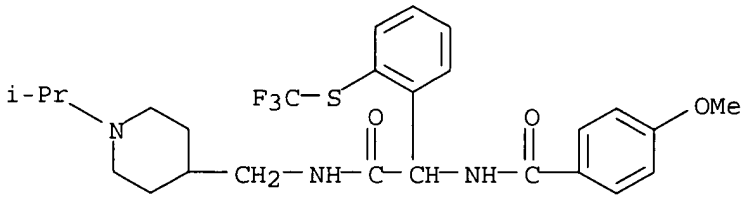
OS MARPAT 136:37947

IT **380900-59-4P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of amino acid derivs. as **serine protease** inhibitors)

RN 380900-59-4 CAPLUS

CN Benzeneacetamide, .alpha.-[(4-methoxybenzoyl)amino]-N-[[1-(1-methylethyl)-4-piperidinyl]methyl]-2-[(trifluoromethyl)thio]- (9CI) (CA INDEX NAME)



AB Compds. R2-X-X-Y(Cy)-L-Lp(D)n [R2 is a 5- or 6-membered arom. carbon ring optionally interrupted by a N, O or S ring atom, optionally substituted at the 3 and/or 4 position or forms a fused ring system at these positions, which is an optionally substituted 5- or 6-membered carbocyclic or heterocyclic ring, or substituted at the position alpha to X-X; X is a C, N, O or S atom or a CO, CR1a, C(R1a)2 or NR1a group, where R1a represents H, OH, alkoxy, alkyl, aminoalkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, alkylaminocarbonyl, alkoxycarbonylamino, acyloxymethoxycarbonyl or alkylamino optionally substituted by OH, alkylamino, alkoxy, oxo, aryl or cycloalkyl; Y is a N atom or a CR1b group (R1b defined as for R1a); Cy is an (un)substituted, (un)satd., mono- or polycyclic, homo- or heterocyclic group; L is an org. linker group contg. 1 to 5 backbone atoms selected from C, N, O and S, or a branched alkyl or cyclic group; -Lp(D)n is 1-[R10-(Lb)u-(G)t-(La)s]-3-pyrrolidinyl or -4-piperidinyl, where s, t and u = 0 or 1; La and Lb is a single bond, CO, O, NH or alkylimino; G = alkanediyl; R10 = alkyl, cycloalkyl, indanyl, pyridyl, tetrahydropyranyl, (un)substituted Ph, etc.] or their physiol.-tolerable salts were prepd. for use as **serine protease** and **factor Xa** inhibitors in the treatment of cardiovascular disorders. Compds. of the invention were found to significantly elongate the partial thromboplastin time (prothrombin time). Thus, 4-[(4-methoxybenzoyl-D-phenylglycinyl)aminomethyl]-1-isopropylpiperidine was prepd. in the first of 106 examples.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	60.28	208.64

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION

CA SUBSCRIBER PRICE -5.86 -5.86

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